PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 334/04342	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/IL05/00074	International filing date *(day/month/year)* 20 January 2005 (20.01.2005)	(Earliest) Priority Date *(day/month/year)* 20 January 2004 (20.01.2004)
Applicant TOPSPIN MEDICAL LTD.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
   ☒ the international search was carried out on the basis of a **translation** of the international application furnished to this Authority (Rule 23.1(b)).
   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2. ☐ **Certain claims were found unsearchable** (See Box I).
3. ☐ **Unity of invention is lacking** (See Box II).
4. With regard to the **title**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   ☐ the text is approved as submitted by the applicant.
   ☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1
   ☒ as suggested by the applicant.
   ☐ because the applicant failed to suggest a figure.
   ☐ because this figure better characterizes the invention.
   ☐ None of the figures

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Box III TEXT OF THE ABSTRACT (Continuation of Item 5 of the first sheet)

A rectal probe for imaging the prostate utilizing both ultrasound and MR imaging modalities, connected by a link. The probe comprises first and second magnetic field sources for generating a static magnetic field and a time-carying magnetic field, respectively, in the imaging region located outside the rectal probe. A receiver is contained within the probe for receiving NMR signals from the excited nuclei and generating MRI data.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC: **A61B 5/00**(2006.01),**5/05**(2006.01)

USPC: 600/407,408,411,424,443

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 600/407,408,411,424,443

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,572,132 A (PULYER et al) 05 November 1996 (05.11.1996), column 1, lines 5-20; column 2, lines 23-64; column 8, lines 49-67; column 9, lines 1-25	1-25
Y	US 5,471,988 A (FUJIO et al) 05 December 1995 (05.12.1995), Figures 47-50; column 43; see entire reference	1-21
Y	US 6,505,063 B2 (VAN DEN BRINK et al) 07 January 2003 (07.01.2003), column 3, lines 45-64; column 4, lines 31-46; column 7, lines 19-60; column 10, lines 60-67; column 11, lines 1-23	13-20
Y	US 5,671,741 A (LANG et al) 30 SeptEMBER 1997 (30.09.1997), column 6, lines 8-24;	20, 22

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
01 May 2006 (01.05.2006)

Date of mailing of the international search report
31 JUN 2006

Name and mailing address of the ISA/US
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Authorized officer
James Kish

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Form PCT/ISA/210 (second sheet) (July 1998)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
PAUL FENSTER
FENSTER & COMPANY, INTELLECTUAL PROPERTY
2002 LTD.
P.O. BOX 10256
PETACH TIKVA, ISRAEL 49002

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	01 JUN 2006
Applicant's or agent's file reference 334/04342	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/IL05/00074	20 January 2005 (20.01.2005)	20 January 2004 (20.01.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC: **A61B 5/00**(2006.01)
USPC: 600/407-408,411,424,443

Applicant

TOPSPIN MEDICAL LTD.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	11 May 2006 (11.05.2006)	James Kish Telephone No. 571-272-5554

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the **language** of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a **sequence listing** and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the **subsequent** or additional copies is identical to that in the application as filed or does not go beyond the application as filed, **as appropriate**, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims NONE	YES
	Claims 1-25	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-25	NO
Industrial applicability (IA)	Claims 1-25	YES
	Claims NONE	NO

2. Citations and explanations:

Please See Continuation Sheet
Claims 1-25 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:
Claims 1-25 lack novelty under PCT Article 33(2) as being anticipated by Pulyer et al. (US Patent No. 5,572,132). Pulyer discloses a MRI probe with a primary magnet having a longitudinal axis and a RF coil, for creating a static magnetic field B_o and RF pulses, respectively and a receiver. A permanent magnet is used to create the static field and could be made to produce any field strength B_o. Surrounding the primary magnet are r-, z-, and phi-gradient coils to provide spatial encoding fields (see Abstract). Depending on the current through the RF coil, any desirable pulse strength could be acquired as well. Also, it is known that attenuation of a magnetic field occurs with an increased distance from the source. The size of the MRI probe will be determined by the particular application to be imaged (column 8, line 49-63). However, Pulyer states that one use of the probe is tissue characterization through transrectal imaging of the prostate (column 2, lines 25-32).

Claims 1-12 lack an inventive step under PCT Article 33(3) as being obvious over Fujio et al. (US Patent No. 5,471,988) in view of Pulyer et al. (US Patent No. 5,572,132). Fujio discloses an ultrasonic that is to be inserted into the rectum to image and treat the prostate. In one embodiment, the probe is fitted with a MR signal receiving high-frequency coil that provides high-resolution internal MRI images (see column 43 and Figures 47-50). These images offer diagnosis of a lesion and determination and setting of treatment area in an even more accurate manner. However, Fujio uses this MR coil with a full MRI system. Pulyer teaches a MRI probe with a primary magnet having a longitudinal axis and a RF coil, for creating a static magnetic field B_o and RF pulses, respectively. A permanent magnet is used to create the static field and could be made to produce any field strength B_o. Depending on the current through the RF coil, any desirable pulse strength could be acquired as well. With respect to claim 3, it is well known that attenuation of a magnetic field occurs with an increased distance from the source. With respect to claim 8-10, Pulyer teaches that slice selective pulses, which are bandwidth-limited pulses, can be generated. While it is not stated that the RF coil is in direct connection with a power supply, it would be obvious to one having ordinary skill in the art that a power supply is needed to produce a RF pulse. With respect to claim 11, Pulyer states that one use of the probe is tissue characterization through transrectal imaging of the prostate. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the probe of Fujio by including magnetic field sources as taught by Pulyer because whole body MRI magnets are very expensive and bulky. They are not particularly portable and, thus, are not generally widely suitable for endoscopical imaging of various parts of the body (column 1, lines 24-27).

Claims 13-19 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of Van Den Brink et al. (US Patent No. 6,505,063). Fujio modified by Pulyer, as described above, teaches an ultrasound and MRI probe combination for imaging the prostate. While it is not disclosed by either reference, it would be obvious that the gradient coils and RF coils in the probe would be connected to a power supply and a controller for controlling the

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

power deliver. Van Den Brink teaches a diagnostic imaging system, notably a MRI system in conjunction with an ultrasound probe. The gradient coils are connected to a controller power supply unit. The gradient coils are energized by applying an electric current thereto by means of the power supply unit. The strength, direction and duration of the gradients are controlled by control of the power supply unit. An MR control unit controls the power supply unit and the transmitter and receiver coils so as to apply the gradient fields and RF excitation pulses (column 7, lines 30-45). A Doppler module is used in conjunction with the system described by Van Den Brink and several images can be taken sequentially with the ultrasound to produce a motion mode (column 10, line 60 through column 11, line 23). Also, it is taught that by acquiring one image, it can be used to improve or correct the other imaging modality (column 3, lines 45-64). With respect to claims 19 and 21, the method claimed in an intended use and the system taught by Van Den Brink is capable of performing this method. It would have been obvious to one having ordinary skill in the art at the time the invention was made to include a power supply and controller for the gradient and RF coils because while the probe is not a conventional MRI system, it would still require any unit or system associated with a conventional MRI system in order to operate properly.

Claims 20-21 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of Lang et al. (US Patent No. 5,671,741). Fujio modified by Pulyer, as described above, teaches an ultrasound and MRI probe combination for imaging the prostate. Van Den Brink teaches to include a power supply and controller for said power supply. However, no discussion on diffusion-weighted MRI is found in these references. Lang teaches a method for differentiating between normal and diseased tissue using diffusion-weighted MRI (column 6, lines 8-24). Also see column 7, line 30 through column 10, line 10. It would have been obvious to one having ordinary skill in the art at the time the invention was made to use a diffusion-weighted pulse sequence as taught Lang with the ultrasound/MRI probe of Fujio and Pulyer in order to provide a proper level of contrast resolution necessary to monitor a cancer patient's response to antitumor treatment, so that treatment-induced tumor necrosis can be adequately measured and quantified (column 1, lines 56-62).

Claims 22-23 lack an inventive step under PCT Article 33(3) as being obvious over Pulyer et al. (US Patent No. 5,572,132) in view of Lang et al. (US Patent No. 5,671,741). Pulyer discloses a MRI probe with a primary magnet having a longitudinal axis and a RF coil, for creating a static magnetic field B_o and RF pulses, respectively. A permanent magnet is used to create the static field and could be made to produce any field strength B_o. Depending on the current through the RF coil, any desirable pulse strength could be acquired as well. However, Pulyer does not discuss diffusion-weighted MR imaging. . Lang teaches a method for differentiating between normal and diseased tissue using diffusion-weighted MRI (column 6, lines 8-24). Also see column 7, line 30 through column 10, line 10. It would have been obvious to one having ordinary skill in the art at the time the invention was made to use a diffusion-weighted pulse sequence as taught Lang with the MRI probe of Pulyer in order to provide a proper level of contrast resolution necessary to monitor a cancer patient's response to antitumor treatment, so that treatment-induced tumor necrosis can be adequately measured and quantified (column 1, lines 56-62).